The Sackler Institute for Developmental Psychobiology

Weill Cornell Medical College

2012-2013

The Sackler Institute maintains a strong reputation in developmental and genomic research, translating transgenic mouse models to human behavior and disease under the leadership of Director and Sackler Professor, Dr. BJ Casey. The faculty and fellows have received several awards (see *Grants and Awards*) and once again published over 50 scientific papers (see *Publications*) during the past year. Training remains a high priority with placement of Sackler fellows in prestigious institutions worldwide (e.g., Harvard), and diversity and training of over two dozen national and international fellows (see *Training and Education*). Outreach activities involve translation of the latest neuroscientific discoveries for the media and policy with coverage by *NPR, PBS, The Wall Street Journal, Forbes Magazine* and *New York Magazine* (see *Outreach Activities*). This report highlights several of the accomplishments of this past year.

Academic Faculty and Staff

Sackler Faculty

B.J. Casey, Ph.D., Director and Sackler Professor of Developmental Psychobiology, WCMC and Adjunct Professor, The Rockefeller University

Barbara Finlay, Ph.D., Adjunct Professor of Psychology in Psychiatry, Cornell University

Michael Posner, Ph.D., Professor of Psychology in Psychiatry, Emeritus, Oregon University

Nim Tottenham, Ph.D., Adjunct Associate Professor of Psychology in Psychiatry, UCLA

Jason Zevin, Ph.D., Associate Professor of Psychology in Psychiatry, WCMC

Sackler Affiliated Faculty

Francis S. Lee, M.D., Ph.D., Professor, WCMC

Charles E. Glatt, M.D., PhD., Associate Professor, WCMC

Sackler Staff

Alisa Powers, Research Coordinator

Jae Woo, M.D., IT Manager

Sackler Predoctoral and Postdoctoral Fellows

Kris Caudle, Ph.D., Postdoctoral Fellow

Ali Cohen, Neuroscience Ph.D. student

Hugo Decker, M.D. Ph.D. tri-institutional student

Andew Drysdale, M.D. Ph.D. tri-institutional student

Cate Hartley, Ph.D., Postdoctoral Fellow

Chelsea Helion, Joint Cornell-Weill Ph.D. student

Aaron Heller, Ph.D., Psychology Intern and Sackler Fellow

Natalie Johnston, Neuroscience Ph.D. student

David Johnson, Neuroscience Ph.D. student

Frederico Lourenco, Neuroscience Ph.D. student

Matthew Malter-Cohen, Neuroscience Ph.D. student

Siobhan Pattwell, Ph.D., Postdoctoral Fellow

Theresa Teslovich, Neuroscience Ph.D. student

Distinguished Sackler Network Scholars

Oana Benga, Ph.D., Babes-Bolyai University, Romania

Sarah Durston, Ph.D., University of Utrecht, The Netherlands

Annette Karmiloff-Smith, Ph.D., Birkbeck, University of London**,** United Kingdom

Urs Maurer, Ph.D., Swiss National Science Foundation, Switzerland

Bruce D. McCandliss, Ph.D., Vanderbilt University, Tennessee, United States

Gaia Scerif, Ph.D., University of Oxford, United Kingdom

Program of Research

The overarching objective of the Institute is to: 1) delineate the biological mechanisms underlying mental health and illness and their development; and 2) to determine the efficacy of innovative therapies and preventive strategies for disorders as a function of developmental status and potential genetic effects inferred from mice and humans. This year, several empirical studies have been completed and published in high profile journals (*PNAS, Nature Communications, Journal of Neuroscience, Annual Review of Medicine, Developmental Science)* using the techniques of brain imaging, human and mouse genetics, psychophysiology, and behavioral methods, to study typical and atypical populations from childhood to adulthood (see *Publications*). Below are highlights from a few studies relevant to communication disorders, substance abuse, anxiety, eating disorders and conduct problems.

1) Communication Disorders

The Institute is involved in a number of basic studies of speech and language led by Dr. Jason Zevin that lay the critical groundwork for the identification, treatment and prevention of communication disorders.

*Speech Perception and Development***.** Dr. Jason Zevin is examining the neural basis of language development, with a specific focus on the development of speech perception in American and Japanese native speakers. Several papers comparing neural responses to native and non-native speech contrasts have been published from this work.

Typical and atypical development of the reading circuit across languages. In collaboration with colleagues at Beijing Normal University and Haskins Laboratories, Dr. Zevin is pursuing

a program of research that combines computational modeling and functional neuroimaging to study how the reading system develops in response to the demands of different writing systems. This work has resulted in a visiting professorship at Beijing Normal University where Dr. Zevin is teaching graduate courses and supervising research studies as part of our collaborative Sackler network.

The role of memory in literacy. Dr. Zevin is examining the role of episodic memory and consolidation in predicting success in literacy acquisition, in collaboration with Kenneth Pugh and colleagues at Haskins Laboratories. They are examining a previously under-studied relationship between individual differences in basic memory processes and literacy skill.

2) Substance Abuse

The Institute is involved in a number of basic studies of self control led by Dr. BJ Casey that lay the critical groundwork for the identification, treatment and prevention of addiction and substance abuse disorders.

Neural Correlates of Delay of Gratification. Dr. Casey with Drs. Mischel and Kevin Ochsner (PI) of Columbia University is using the delay of gratification, appetitive go/nogo and emotion regulation tasks that they have each developed to understand the development of neural mechanisms that enable us to regulate the appetitive pull of potentially unhealthy substances (e.g., fattening foods or drugs) and the aversive push of unpleasant emotions that might motivate one to seek these substances in the first place. This work is funded by a collaborative grant by NICHHD (PI: Ochsner).

Goal-oriented and Habitual Action Selection. Dr. Hartley, under the mentorship of Drs. Casey and Glatt and Dr. Bruce McEwen at The Rockefeller University submitted a K99 application to NIH to study the neuromodulation of goal-oriented and habitual action selection across development and as a function of stress. Habitual action selection has been implicated in substance abuse and addiction.

3) Anxiety Disorders

The Institute is involved in a number of basic studies of emotion that merges basic, human and clinical research by Drs. Francis Lee, Charles Glatt, John Walkup and Casey that lay the critical groundwork for the identification, treatment and prevention of anxiety disorders.

SERT (rs3813034) and Fear Extinction Retention. Postdoctoral Fellow Dr. Cate Hartley, in collaboration with Drs. Glatt and Casey and Dr. Liz Phelps of NYU published a study examining how two polymorphisms (Hartley et al 2012 *PNAS*) tied to variation in 5-HTT expression are associated with differences in extinction retention. The 5-HTT KO mouse shows impaired extinction retention. The results suggest that genetically-mediated differences in extinction retention may be associated with risk for anxiety.

Development of Extinction. Dr. Siobhan Pattwell and Dr. Stephanie Duhoux, fellows of Drs. Casey and Lee published a study examining the development of extinction-related behavior in pre-, peri- and post adolescent mice and humans in *PNAS* (Pattwell et al. 2012). They showed less extinction learning and less infralimbic activity in adolescents. These findings have significant implications as to when exposure therapy may be most beneficial for treatment of anxiety disorders given that exposure therapy relies on principles of extinction reported by Casey, Pattwell, Glatt & Lee in the *Annual Review of Medicine* this year.

Translational Studies of Anxiety. MD, PhD student Andrew Drysdale in collaboration with Drs. Casey, Lee and Walkup have submitted a translational perspective paper to *JAACAP* that provides proof of principle for when to treat children with anxiety disorders based on developmental human and mouse preclinical studies.

Placebo Effects across Development. M.D., Ph.D. candidate Hugo Decker under the mentorship of Casey, is examining the development of the placebo effect. The placebo effect appears to be larger in children than adults, especially in clinical trials for depression. Given the prefrontal cortex has been implicated in placebo effects, and this region is fairly immature in children, he will examine the neural correlates of the placebo effect across development to better understand its neural basis.

4) Eating Disorders

The Institute is involved in a number of collaborative studies with Columbia University on eating behavior led by Drs. Casey and Glatt that lay the critical groundwork for the identification, treatment and prevention of eating disorders.

Caloric Restriction Enhances Fear Extinction Learning in Mice. MD, PhD candidate Megan Riddle under the mentorship of Dr. Glatt has examined the effects of diet restriction on anxiety behaviors. A common antecedent to Anorexia Nervosa is anxiety. They have shown that diet restriction decreases anxiety and may explain one pathway to anorexia. These findings were published this year in *Neuropsychopharmacology*.

Genetic Studies of Obesity. Dr. Casey, together with PIs Rosenbaum & Mayer from Columbia NYSPI, received a R56 grant entitled *Functional imaging and eating behavior among FTO genotypes in pre-obese children* and submitted a follow-up five-year R01 application in March 2013. This joint institution collaboration involves a genetic imaging study of obesity in children focusing on the effect of the FTO gene and neural circuitry underlying sensitivity to food cues in children using behavioral paradigms developed at the Institute.

Delay of Gratifictaion and Anorexia Nervosa. Drs. Casey and Kris Caudle are involved in a collaborative study funded by the Klarman Foundation to examine neural correlates of delay of gratification, discounting and impulse control in Anorexia Nervosa with Drs. Tim Walsh and Joanna Steinglass (PI), both at Columbia NYSPI.

Sensitivity to Reward and Emotional Cues in Bulimia. Dr. Casey is collaborating with investigators at Columbia (Allegra Broft and Tim Walsh) on an imaging study of Bulimia Nervosa to identify neural circuitry underlying sensitivity to emotional, reward and food cues in this patient population. This work is being submitted as an RO1 application to the NIH and uses behavioral paradigms developed at the Institute.

5) Conduct Disorders

The Institute is involved in a number of collaborative studies on conduct and criminal behavior led by Dr. Casey that lay the critical groundwork for understanding the emergence of aggression and criminal behavior during development.

Law and Neuroscience. Dr. Casey is the PI of a multisite (WCMC, UCLA, Temple, and OSHU) MacArthur Foundation funded study to examine neural correlates of criminal-related

behavior in adolescents. A special issue of Current Directions in Psychological Science that Casey edited, highlighted this area of work and came out April 2013.

Emotion Dysregulation and Conduct Disorders. Dr. Casey submitted an R01 application to examine how acute and sustained threat can lead to reactive and avoidant behavior. Neural correlates of these two common forms of emotion dysregulation (anxiety and conduct problems) are being examined with functional imaging.

Education and Training

A significant objective of the Institute is in training, education and outreach. The Institute's network has international collaborations established with China and the Netherlands in addition to national ones with Cornell, Columbia, Connecticut, NIMH, NYU, UCLA, Vanderbilt, Wash U, Temple University, University of Pennsylvania, Princeton, Rockefeller, Stanford, UC Irvine, UCSD, Scripps, University of Hawaii, MGH and Yale. Highlights of the Institute's training activities are provided below.

Mortimer D. Sackler, MD Summer Institute. Last year marked the first summer institute since it was renamed, the Mortimer D. Sackler, M.D. Summer Institute and supported by a generous gift from the Sackler family. The course was co-directed by Drs. Casey and Bill Fifer of the Sackler Institute at Columbia University and held in New York City and focused on learning and plasticity. Twenty of nearly 100 applicants were selected from around the world. This year's course will focus on learning and decision-making and has an all-star line-up of previous summer institute participants who are now leaders in the field of developmental and cognitive neuroscience.

Residency Education. Dr. Casey has played a significant role this year in teaching both adult and child psychiatry residents at Weill Cornell Medical College as part of the Residency program curriculum.

Brain and Mind. Drs. Casey and Pattwell played significant roles this year in teaching medical students at Weill Cornell and Weill Qatar about developmental neuroscience by providing lectures and labs for the students that have resulted in participation of the medical students in rotations and Sackler seminars.

Neuron to Brain. Drs. Casey and Pattwell played significant roles this year in teaching Weill Cornell Biomedical Graduate Program in Neuroscience courses that link brain and behavior.

Ithaca-Weill Joint Graduate Program in Development and Learning. Dr. Casey, in collaboration with Dr. Barbara Finlay of Cornell University-Ithaca, co-directed an NICHHD T32 funded joint institutional interdisciplinary training grant submission for predoctoral fellows in development and learning (see http://neuroscience.cornell.edu/imagine.html).

Recruitment of Underrepresented Minorities. Dr. Casey participates in the Gateway and Access programs that provide summer mentorship for underrepresented minorities who may be potential MD, PhD and PhD applicants to Weill Cornell. Currently she mentors two minority fellows.

Outreach Activities

This year has been a significant one for outreach related activities in local, national and international settings. We provide a few examples of these efforts below.

Neuroscience and the Law. Dr. Casey is part of a PBS Special that airs this year on "Brains on Trial" narrated by Alan Alda. In addition, Dr. Casey co-wrote the IOM report on Juvenile Justice Reform. She has provided educational lectures as part of symposia and conferences on law and neuroscience at the Society for Cognitive Neuroscience in San Francisco, the NYU Institute of Human Development and Social Change Forum on Violence and Schools in New York and the MacArthur Foundation Research Network on Law and Neuroscience sponsored workshops on Future of Law and Neuroscience in Chicago, all in April 2013.

IOM and NAS National Council for Research (NCR). Dr. Casey has rotated off the Board of Children, Youth and Families as an expert in developmental neuroscience, but is serving on the NCR committee on *Concussions in Youth Sports* that will come out next year

Education. Dr. Casey sits on the Board of two New Vision Schools based on the Bronx JFK high school campus.

Public. Dr. Casey sits on The Rockefeller University/Parents & Science Program and will be speaking next spring on the teenage brain.

Media Publicity. Research by Dr. Casey and others at the Sackler Institute has been covered by NPR: *Teens wait rather than react impulsively when rewards are at stake*, PBS: *Brains on Trial*, Live Science: *Secret to Self-Control: A More Efficient Brain?,* New York magazine: *Why You Truly Never Leave High Scho*ol, Science News for Kids: *The teenage brain*, Discovery News: *The Teen Brain on Rage: How it's Different*, Wall Street Journal: What's Wrong With the Teenage Mind? Post-doctoral Fellow, Dr. Siobhan Pattwell, was honored in Forbes magazine for her work in adolescence and anxiety (Forbes "30 Under 30" in Science & Healthcare). See http://www.sacklerinstitute.org/cornell/sackler_in_the_news/

Special Issue of Current Directions in Psychological Science on The Teen Brain. Dr. Casey edited a special issue of this journal that highlights what we have learned about the teen brain from imaging and nonhuman animal studies that came out in April 2013.

Grants and Awards

Grants and Awards (2012-2013)

Dr. Casey was appointed as an NIMH Council member.

Dr. Casey gave the 2012 Salmon Lecturer and Dr. Posner was the Salmon Medalist for 2012.

Dr. Casey received the 2012 Excellence in Teaching Award from the Medical College. This award acknowledges her teaching and service to the college over the past 10 years.

Dr. Casey received the Douglas Powers Visiting Scholar Award from Vanderbilt University for her exceptional mentoring.

Dr. Casey was invited to give a Master lecture at the biennial meeting of the Society for Research on Child Development, in April, 2013.

Dr. Casey, in collaboration with investigators at Columbia (Laurel Mayer and Michael Rosenbaum), received a R56 on a genetics imaging study of obesity in children focusing on the effect of the FTO gene and neural circuitry underlying sensitivity to food cues in children.

Dr. Glatt was appointed Director of the Genetics Core at the Conte Center at Columbia University (PI: Gingrich). His role is as the PI of the Genetics Core supervising the collection, data basing and analysis of human genetic samples for projects that involve human genetic analysis (Projects 2 and 3). He will also coordinate with investigators in Project 4 involving analysis of rhesus genetic variation and mouse behavioral analyses.

Dr. Hartley received an honorable mention for the 2012 NYAS James McKeen Cattell Award for Outstanding Dissertation in Psychology.

Dr. Hartley received the 2013 Samuel W. Perry III, M.D. Distinguished Award in Psychiatric Medicine.

Chelsea Helion, a PhD student, received a research grant from Cornell University Psychology department and a travel reward grant from Cornell University Schools of Arts and Sciences.

Dr. Pattwell was awarded The Brain & Behavior Research Foundation NARSAD Young Investigator Award. The project looks into persistent attenuation of conditioned fear memories across development.

Dr. Pattwell was named as a Forbes "30 Under 30" in Science/Healthcare.

Dr. Somerville was awarded an NIMH R00 Independent Phase grant as transitioned from Sackler postdoctoral fellow to a tenure track faculty member at Harvard. She will look at the development of tonic and phasic neural systems mediating affect and anxiety.

Dr. Somerville received the 2013 Association for Psychological Science Rising Star Award.

Dr. Tottenham was awarded a grant from the Dana Foundation. She will be researching the epigenetic restructuring of Human DNA following early-life stress.

Dr. Zevin received an R43 grant as co-PI in collaboration with Perception Research Systems. The project involves developing and testing a hardware solution to connectivity issues for stimulus presentation and scanner synchronization at multi-user MR centers.

Dr. Zevin will act as Director of the Modeling Core for a P01 grant studying the Nature and Acquisition of the Speech Code (PI: Rueckl). The study investigates phonological competence in speech and reading from acquisition of early speech abilities up through extended discourse comprehension.

Dr. Zevin was admitted to be a Visiting Fellow at the Chinese Academy of Sciences (Young International Scientists) program.

The Institute directly, and in collaboration with others, has grants and awards from NSF, NIMH, NIDA, NIDCD, the Dewitt Wallace Readers Digest, and the John Merck Fund. This funding supplements the generous gifts by the Mortimer D. Sackler, M.D. family.

Pending Grants and Awards

Dr. Casey submitted an R01 application to examine how acute and sustained threat can lead to reactive and avoidant behavior.

Dr. Casey submitted an R01 application that involves a genetic imaging study of obesity in children focusing on the effect of the FTO gene and neural circuitry underlying sensitivity to food cues in children.

Dr. Hartley submitted a K99 application to NIMH to study the neuromodulation of goal-oriented and habitual action selection across development.

Dr. Hartley submitted a NARSAD application to study the effects of stress on goal-oriented and habitual action selection.

Dr. Zevin was included as Co-Investigator on a P01 application submitted to NICHD by Robin Morris (co-PI, GA Tech), Maureen Lovett (co-PI, Hospital for Sick Children) and Kenneth Pugh (co-PI, Haskins Labs). The project will use a well-respected intervention program for reading disability to identify "non-responders" and examine their profiles on a set of general measures of language and memory processing abilities.

Publications

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